
Circulating tumor cells exhibit metastatic tropism and reveal brain metastasis drivers.

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Public Summary:

Scientific Abstract:

Hematogenous metastasis is initiated by a subset of circulating tumor cells (CTCs) shed from primary or metastatic tumors into the blood circulation. Thus, CTCs provide a unique patient biopsy resource to decipher the cellular subpopulations that initiate metastasis and their molecular properties. However, one crucial question is whether CTCs derived and expanded ex vivo from patients recapitulate human metastatic disease in an animal model. Here, we show that CTC lines established from breast cancer patients are capable of generating metastases in mice with a pattern recapitulating most major organs from corresponding patients. Genome-wide sequencing analyses of metastatic variants identified semaphorin 4D (SEMA4D) as a regulator of tumor cell transmigration through the blood-brain-barrier and MYC as a crucial regulator for the adaptation of disseminated tumor cells to the activated brain microenvironment. These data provide the direct experimental evidence of the promising role of CTCs as a prognostic factor for site-specific metastasis.

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